The Egyptian Journal of Neurology, Psychiatry and Neurosurgery

RESEARCH

Open Access

Factors predicting functional outcome after rtPA for patients with acute ischemic stroke

Yasser Hamed[1,2†], Mahrous I. Seddeek[3,4*†], Ali Mahmoud Ahmed[3,5*†], Talal A. Dawa[3,4], Hasan Hashem[1,6], Adel M. Othman[7,8], Abdel-Ghaffar I. Fayed[3], Noran Elbazzar[2,9], Ramy A. Metwally[2,9], Mostafa El Sayed Abd Elghany El Sayed[2,10], Ahmed Yousry[2,11] and Abd Elaziz Shokry[1]

Abstract

Background Accurate outcome prediction for patients with acute ischemic stroke after intravenous recombinant tissue plasminogen activator (rtPA) treatment is essential for optimizing patients' management. We aimed to identify factors associated with unfavorable outcomes following intravenous rtPA treatment. This study was carried out on 162 patients who presented with acute ischemic stroke within 4.5 h from onset of neurological symptoms and were eligible for intravenous rtPA. After exclusion of 48 patients, 114 patients were finally eligible for follow-up. After complete medical and neurological history, complete medical and neurological examination and brain image (CT and or MRI brain) were collected from the patients. patients eligible were included in the study. NIHS scale was assessed for all patients at time of admission, after 24 h, and follow-up for 3 months.

Results After a 90-day follow-up period for 114 patients with acute ischemic stroke after rtPA, 35.8% had good outcome (MRS; 0–2), 18.5% had partial outcome (MRS; 3–4) and 12.5% had poor outcome (MRS; 5–6). Atrial fibrillation (AF), PH of stroke, stroke severity, and severity of symptom (NIHSS) score were significantly (*P*: 0.004, 0.001, 0.007 and 0.001) correlated with poor outcome after rtPA. Similarly, old age, high blood pressure at time of presentation, hypertension, and dyslipidemia were showed to carry poor outcome.

Conclusions AF, high NIHSS score, PH of stroke, previous stroke, hypertension, dyslipidemia, and high blood pressure on presentation were significantly correlated with poor functional outcome.

Keywords Stroke, rtPA, NIHSS, MRS, AF

†Yasser Hamed, Mahrous I. Seddeek and Ali Mahmoud Ahmed have contributed equally to the study.

*Correspondence:
Mahrous I. Seddeek
mahrousseddeek@azhar.edu.eg
Ali Mahmoud Ahmed
ali.m.ahmed@azhar.edu.eg
[1] Department of Neurology, Faculty of Medicine, Al-Azhar University, Assiut, Egypt
[2] Department of Neurology, Al Jedaani Group of Hospitals, Jaddah, Kingdom of Saudi Arabia
[3] Department of Neurology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[4] Department of Neurology, Dallah Hospitals, Riyadh, Kingdom of Saudi Arabia
[5] Department of Neurology, The Royal Wolverhampton NHS Trust, Wolverhampton, UK
[6] Department of Neurology, Specialized Medical Center Hospitals, Riyadh, Kingdom of Saudi Arabia
[7] Department of Neurology, Faculty of Medicine, Al-Azhar University, Damitta, Egypt
[8] Department of Neurology, Saudi German Hospitals, Riyadh, Kingdom of Saudi Arabia
[9] Department of Internal Medicine, Benha University, Benha, Egypt
[10] Department of Cardiology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[11] Department of Cardiology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Background

Stroke is one of the most frequent causes of death and disability in developed countries, having an estimated overall adult prevalence of 2.5% [1]. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017 showed that stroke was the third-leading cause of death and disability combined and the second-leading cause of death worldwide in 2017 [2, 3]. Treatment on specialized stroke units is essential in secondary prevention leading to an 18–46% reduction of relative mortality and 29% reduction of assistance-depending disability [4]. Rapid administration of intravenous recombinant tissue-type plasminogen activator (rtPA) to appropriate patients remains the mainstay of early treatment of acute ischemic stroke [5]. The benefit of the treatment diminishes significantly and is lost after 4.5 h [5].

The benefit of intravenous thrombolysis for acute ischemic stroke decreases continuously over time from symptom onset, as shown in meta-analyses of randomized trials [6, 7]. However, there is still large proportion of patients with unfavorable outcome after IV rtPA treatment [8]. Accurate and early prediction of the clinical outcome for individual AIS patients who receive rtPA treatment is needed to provide a reasonable approach to patient management [9].

It is well-known that factors, such as age, initial NIHSS score, and systolic blood pressure, are of predictive value for clinical outcome and symptomatic intracerebral hemorrhage (SICH) [6]. Magnetic resonance imaging (MRI), computed tomography (CT), and carotid duplex have also been used as possible prognostic determinant tools. Particularly, many factors, including arterial occlusion, re-occlusion, and recanalization among other factors, have been reported to have predictor effect [10]. This study was prospective aimed to identify factors associated with unfavorable outcome following intravenous rtPA treatment.

Methods

The study was carried out as a prospective observational cohort study on 162 patients presented with acute ischemic stroke aged between 18 and 80 years and who presented in the first 4.5 h time window from the onset of stroke symptoms attended the Neurology Department of Al Jedaani Hospitals, KSA during the period from February 2019 to the end November of 2022. 10 patients were expired (six patients due to massive intracerebral hemorrhage as adverse effect of rtPA and four patients from extensive infarction), about 38 patients were shifted to another hospital for endovascular treatment, and remaining 114 patients completed follow-up for 3 months (Fig. 1).

This study has been approved by ethical committee of Aljedaani Hospitals belong of Ibn Sina faculty of medicine hospitals, KSA. All patients eligible for rtPA were included in the study. Eligibility criteria and contraindications for IV rtPA at our study were the same as those Guidelines for the Early Management of Patients with Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association [11]. Patients who did not received the full dosage of IV rtPA due to acute adverse side effect during infusion, patients did not complete follow-up for 3 months or patients who refused participation in the study were omitted.

After complete medical and neurological history (age, sex, body weight, height, body mass index (BMI), smoking status, history of hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, atrial fibrillation and past history of stroke) and examination (initial National Institutes of Health Stroke Scale (NIHSS) score (NIHSS score before rtPA and 24 h after rtPA, admission SBP and DBP (patients with SBP higher than 185 were lowered by IV Na nitroprusside to lower than 185 before start rtPA), CT brain and or MRI brain (at time of admission and 24 h after infusion of rtPA), cardiac workup (ECG, Echocardiography, troponin, CK mb), carotid duplex and some laboratory (hemoglobin, white blood cell count, platelet count, capillary blood glucose at presentation, fasting blood glucose, hemoglobin A1C (HbA1C), lipid profiles and prothrombin time) were done for all patient immediately at time of arrival. The etiologic classification of stroke was conducted according to TOAST classification [12]. All patients were administered with standard dose IV rtPA 0.9 mg/kg (adjusted by weight of patient, maximum 90 mg, 10% of dose IV bolus and remaining 90% IV infusions over 1 h) within 4.5 h of symptom onset, based on United States Food and Drug Administration-approved indications [13].

Stroke severity was categorized based on NIHSS and the size of the infarction into mild stroke, when the NIHSS score ≤ 8 with lacunar infarction or small vessel disease; moderate stroke when the NIHSS score 9 to 15 with infarction less than third of the brain; and severe stroke when the NIHSS score ≥ 16 with massive infarction more than the third of the brain [14].

The follow-up assessment was conducted after 3 months from the stroke onset. The primary outcome measures the functional outcome according to Modified Rankin Score (MRS). It was classified into good outcome (MRS scores of 0–2), partial outcome (MRS scores of 3–4) and poor outcome (MRS scores of 5–6) that indicating major disability or death [15].

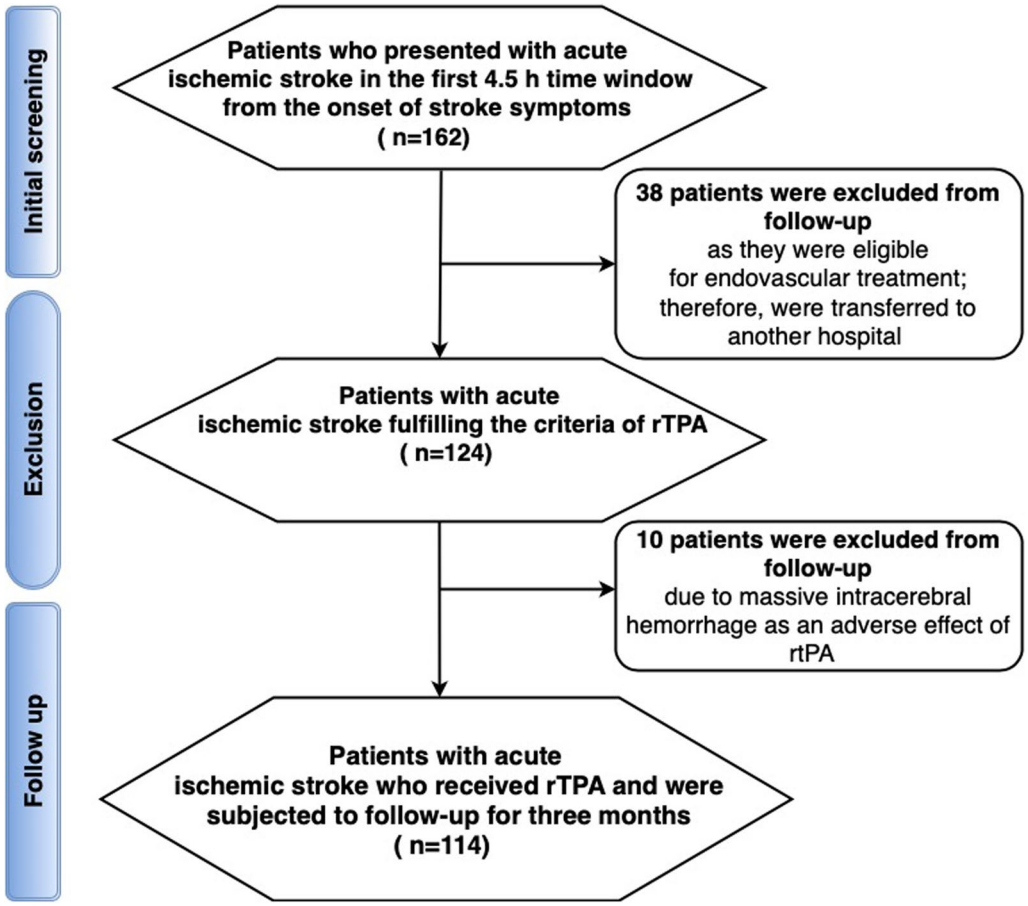

Fig. 1 Flow diagram of all included patients showing the selection of the included patients for follow-up and the omitted patients

Hemorrhagic transformation post thrombolysis was graded according to the ECASS I (European Cooperative Acute Stroke Study I) criteria [16]. Symptomatic intracerebral hemorrhage (SICH) was defined as the presence of intracerebral hemorrhage with worsening of NIHSS score by > 4 points occurring within 48 h of administration of rtPA [16]. Delayed hemorrhage was defined as intracerebral hemorrhage occurring ≥ 48 h after the administration of rtPA [17]. Mortality due to any cause was also recorded.

Appropriate statistical methods were applied and the results were tabulated and presented accordingly. $P < 0.05$ was considered significant.

Results

The study was carried out on 162 patients (136 males and 26 females) with mean age 60.43 ± 12.094 presented with acute ischemic stroke with duration of symptoms less than 4.50 h from onset of neurological symptoms. All patients were candidate for rtPA and received full dose of rtPA adjusted by weight of patient. The prevalence of hypertension, diabetes mellitus, hypercholesterolemia, cardiac disease, AF, PH of stroke, obesity and smoking were 56.8%, 43.2%, 45.7%, 48.2%, 30.86%, 3.7%, 16.2%, and 35.8%, respectively (Table 1).

Table 1 Demographic data of the studied patients

Variable	*P* value*
Sex (male)	136 (84%)
Age (mean ± SD)	60.43 ± 12.094
Comorbidities	
HTN	92 (56.8%)
DM	72 (43.2%)
Dyslipidemia	74 (45.7%)
Cardiac disease	78 (48.2%)
Obesity	26 (16.2%)
Smoking	58 (35.8%)
AF	50 (30.86%)
PH of stroke	6 (3.7%)

HTN hypertension, *DM* diabetes mellitus, *AF* atrial fibrillations, *PH* past history

*Data were presented as number and frequency except the age was presented and mean ± standard deviation

Table 2 Clinical presentation of the studied patients

Variable	Number	Percent
Side		
Right	118	72.8%
Left	44	27.2%
Degree of stroke		
Mild	4	2.5%
Moderate	28	17.3%
Severe	130	80.2%
Duration (hours) (mean ± SD)	2.32 ± 0.79	
NIHS scale (mean ± SD)	20.16 ± 4.08	

NIHS scale National Institute of Health Stroke Scale

Table 3 Outcome after rtPA according to Modified Rankin Scale (MRS)

Outcome	Number (percentage)
Good outcome (scores 0–2)	58 (35.8%)
Partial outcome (scores 3–4)	30 (18.5%)
Poor outcome (scores 5–6)	22 (12.5%)
Hemorrhage	14 (8.6%)
Referred for thrombectomy	38 (23.5%)

Regarding to clinical presentation, most of patients (72.8%) presented with right side hemiplegia and duration of symptoms was 2.32 ± 0.79. The degree of stroke was 80.2% of patients had severe degree, 17.3% had moderate and remaining 2.5% had mild degree. The NIHS scale at time of admission was 20.16 ± 4.08 (Table 2). After administration of rtPA, 8.6% complicated with hemorrhage and 23.5% had no response at all and MR angiography showed large artery occlusion and referred to another hospital for endovascular thrombectomy. Remaining 66.8% of patients follow-up for 3 months and outcome was 35.8% had good outcome (MRS; 0–2), 18.5% had partial outcome (MRS; 3–4) and 12.5% had poor outcome (MRS; 5–6). Old age patients, hypertensive patients and hypercholesterolemia had poor outcome (Table 3).

Discussion

Ischemic stroke is highly prevalent worldwide. Thrombolysis has been found to be the most effective medical treatment for acute ischemic stroke (AIS) patients [18]. Unfortunately, some patients still experience functional deficits after rtPA thrombolysis. Accurate and early prediction of the clinical outcome for individual AIS patients who receive rtPA treatment is needed to provide a reasonable approach to patient management [9]. The present study was a prospective observational study aimed to study the predictors for favorable and unfavorable outcome of stroke patients after rtPA (Tables 4, 5).

The prevalence of hypertension, diabetes mellitus (DM), hypercholesterolemia and dyslipidemia, cardiac disease, AF, past history (PH) of stroke, obesity and smoking in our study were 56.8%, 43.2%, 45.7%, 48.2%, 30.86%, 3.7%, 16.2%, and 35.8%, respectively, came in partial agreement with Emad et al. [19], they concluded the prevalence of HTN, DM, Dyslipidemia, IHD and smoking

Table 4 Correlation between demographic data and outcome after rtPA based on Modified Rankin Scale (MRS)

Demographic variable	Functional outcome based on MRS			Hemorrhage No = 14	Referred for thrombectomy No = 38	*P* Value **
	Good No = 58	Partial No = 30	Poor No = 22			
Sex						
Male	46	30	18	12	30	0.443
Female	12	0	4	2	8	
Age (mean ± SD)	59.3 ± 8.6	58.9 ± 13.7	66.5 ± 12.6	58.8 ± 15.1	61.9 ± 14.4	0.489
Risk factors						
HTN	51.7%	40%	81.8%	71.4%	57.9%	0.628
DM	27.6%	46.7%	54.5%	42.9%	57.9%	0.267
Dyslipidemia	37.9%	26.7%	72.7%	28.6%	52.6%	0.09
Cardiac	41.2%	40%	63.6%	42.9%	57.9%	0.594
Obesity	20.7%	00%	18.2%	42.9%	10.5%	0.11
Smoking	27.6%	53.3%	36.4%	57.1%	26.3%	0.288
AF	13.8%	40%	27.3%	14.3%	57.9%	0.004
PH of stroke	00%	00%	00%	42.9%	00%	0.001

HTN hypertension, *DM* diabetes mellitus, *AF* atrial fibrillations, *PH* past history

**P* value was considered significant if it was <0.05

Table 5 Correlation between clinical presentation and outcome after rtPA based on Modified Rankin Scale (MRS)

Clinical presentations	Functional outcome based on MRS			Hemorrhage No = 14	Referred No = 38	*P* value*
	Good No = 58	Partial No = 30	Poor No = 22			
Side						
Rt	34	26	16	6	36	0.016
Lt	24	4	6	8	2	
Degree of stroke						0.007
Mild	4	0	0	0	0	
Moderate	16	8	3	1	0	
Severe	38	22	19	13	38	
Duration (mean ± SD)	2.26 ± 0.93	2.6 ± 0.34	1.68 ± 0.67	2.7 ± 0.49	2.32 ± 0.85	0.108
BP (Mean ± SD)	162 ± 26	161 ± 25	188 ± 31	163 ± 27	169 ± 28	0.101
NIHS scale (Mean ± SD)	17.17 ± 4.29	20.13 ± 2.33	22.36 ± 3.36	24 ± 2.67	22.0 ± 2.36	0.001

NIHS scale National Institute of Health Stroke Scale, *BP* blood pressure

**P* value was considered significant if it was < 0.05

were 58%, 43%, 45.8%, 42%, and 30%, respectively, and with Masoud et al. [20], they reported prevalence of hypertension, diabetes mellitus, dyslipidemia, cardiac disease, AF, PH of stroke and smoking were 69.5%, 34.7%, 23.7%, 46.6%, 20.3%, 21.2% and 21.2%, respectively. The prevalence of AF in our study was higher than other both studies, because all patients with chronic AF eligible for rtPA, newly diagnosed AF at time of stroke and patients with paroxysmal AF were included.

Our study like many studies [19–22] showed a highly significant association between the severity of stroke, assessed by NIHSS score and infarction size on admission and an unfavorable outcome was detected ($P = 0.007$). The NIHSS score was a good predictor of stroke outcome and that a remarkable neurologic impairment assessed by NIHSS score was associated with less favorable outcome The NIHSS score is significantly and strongly correlated with poor outcome after rtPA for acute ischemic stroke.

In addition to stroke severity, past history of stroke was associated with poor outcome and increase risk of SICH and this result agree with Wafaa [23] who reported the same results, while other studies [20, 24] reported no significant correlation between history of previous stroke and poor outcome. Patient who had recurrent stoke commonly had multiple risk factors for stroke, poor control of risk factors, poor compliance on medications and advanced atherosclerosis that have unfavorable outcome after rtPA.

Regarding patients with AF, our study showed significant ($P = 0.004$) correlation to poor outcome, this result came in agreement with previous literature [20, 25–28]. All of the previous studies reported significant correlation between AF and poor outcome after rtPA and concluded that it is mostly due to high incidence of associated SICH. The thrombus formed in AF patient was formed inside heart and carried with blood to brain; it may take time inside heart makes it hard thrombus and difficulty to dissolve by fibrinolytic effect of rtPA. Other studies [19, 23] reported that no significant correlation between AF and outcome. The presence of AF among these studies were very low (5/131 and 7/40, respectively). The exact mechanisms of AF on the outcomes of stroke patients were not clear, and stroke patients with AF may have large and old thrombi, which are not sensitive to the treatment of thrombolytic therapy [29].

Regarding to blood pressure at time of presentation, the result of our study showed that patients with high blood pressure at time of presentation carried poor outcome that agree with Leonardi Bee et al. [30] and Okumura et al. [31], they reported that patients presenting with AIS who have an extremely elevated BP have worse outcomes, which is likely due to the baseline increased severity in stroke symptoms. Darger et al. [32] reported that there was a statistically significant difference in adverse events between patients requiring any method of BP control prior to thrombolysis versus those who did not, when adjusting for the baseline severity of the stroke. Previous studies have revealed that both high and low blood pressure were independent prognostic factors for poor outcome in ischemic stroke patients [30, 33].

Regarding to risk factors of stroke, results of our study showed that, the patient had hypertension, dyslipidemia and ischemic heart disease carried poor outcome and high risk for ICH. Bhardwaj et al. [34], who found that risk factors such as hypertension, diabetes, dyslipidemia, smoking, alcohol intake, coronary artery disease and valvular heart disease did not influence outcome in patients of acute ischemic stroke receiving

rtPA [34]. Patients with chronic hypertension have shifts in perfusion autoregulation parameters as well as changes in collateral blood supplies and this, in conjunction with other considerations, such as carotid artery stenosis, put hypertensive stroke patients at a unique risk special consideration should be considered when determining rtPA eligibility in these patients [35, 36].

Our study showed significant negative correlation between DM and the functional outcome. This was present in the univariate analysis and when tested as independent predictors of the functional outcome among risk factors using the multivariate analysis, it was a strong independent predictor of poor functional outcome. This was in agreement with many studies which had identified DM as a predictor of poor functional outcome after receiving IV rtPA among stroke patients like that conducted by Roquer and et al. [37] and that was conducted by Saposnik et al. [38]. However, other studies did not show significant correlations between DM and functional outcome after receiving IV rtPA, but had showed a significant correlation between admission hyperglycemia and poor functional outcome after receiving IV rtPA [37, 39]. Our study showed non-significant correlation between smoking and the functional outcome 3 months after receiving IV rtPA, and this was in agreement with previous studies [39, 40]. In contrary to other studies which revealed significant negative correlation between recent or current smoking and functional outcome 3 months after IV rtPA [41].

In addition to modifiable risk factors of stroke, age is one of the major determinants of stroke outcomes [38, 42]. Elderly patients were prone to have poorer outcomes compared with young patients after rtPA thrombolysis treatment [43, 44]. Besides, elderly patients were more likely to have complications, such as AF and hypertension, as well as higher NIHSS score, all of which may influence stroke outcomes [44, 45]. In the present study, patients with an unfavorable outcome had a higher median age than those with a favorable outcome; the effect of age on outcome was not significant after adjusting for confounding variables.

Despite this study illustrated the factor associated with post-rtPA outcomes, it has some limitations. One of these limitations is the small sample size of the included patients that did not enable us to make more advanced statistical analysis. In addition, the shortness of the follow-up duration may be a contributing factor that prevent some clarity in the association. It is known that, the MRS improves with time after stroke; therefore, the time provide a chance for positive outcome. Moreover, we did not use the serum stroke biomarkers to test their association with post-stroke functional outcomes.

Conclusions

AF, PH of stroke, stroke severity, and severity of symptom (NIHSS) score were significantly correlated with poor outcome after rtPA. In addition, old age, high blood pressure at time of presentation, hypertension, dyslipidemia were the demographics that carried poor outcome. Patients with acute ischemic stroke who are eligible for rtPA and have one or more of these variables should be monitored carefully on both short and long term.

Abbreviations

rtPA	Recombinant tissue plasminogen activator
GBD	Global Burden of Diseases
SICH	Symptomatic intracerebral hemorrhage
MRI	Magnetic resonance imaging
CT	Computed tomography
HbA1C	Hemoglobin A1C
MRS	Modified Rankin Score
NIHSS	National Institutes of Health Stroke Scale
ECASS1	European Cooperative Acute Stroke Study I
HTN	Hypertension
DM	Diabetes mellitus
AF	Atrial fibrillations
PH	Past history
BP	Blood pressure

Acknowledgements

Not applicable.

Author contributions

YH, MIS, and AMA participated in hypothesis generating, data collection, data analysis, and manuscript writing. TAD, HHA, AMO, AIF, and AS proposed the idea, tested the hypothesis, and revised the extracted data, data analysis and manuscript. NE, EAM, MEAE, and AY participated in hypothesis generating, data collection, data analysis, and manuscript writing. `All authors have read and approved the manuscript.

Funding

This study was self-funded by the authors.

Availability of data and materials

The data sets analysed during the current study are not publicly available as the participants requested that, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in concordance with declaration of Helsinki and each participant signed a written informed consent before being enrolled in the study. The institutional review board (IRB)approval was obtained from the ethical committee of Aljedaani Hospital on 14th January, 2019. There was no reference number provided by our IRB.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 24 June 2023 Accepted: 12 January 2024
Published online: 07 February 2024

References

1. Thom T, Heart disease and stroke statistics. 2006 update: a report from the American heart association statistics committee and stroke statistics subcommittee. Circulation. 2006;113:e85–151.
2. Kyu HH, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392:1859–922.
3. Krishnamurthi RV, Ikeda T, Feigin VL. Global, regional and country-specific burden of ischaemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage: a systematic analysis of the global burden of disease study 2017. Neuroepid. 2020;54:171–9.
4. Maiera LM, Bauerleb P, Kermera C, Helms HJ, Buettner T. Risk prediction of very early recurrence, death and progression after acute ischaemic stroke. Eur J Neurol. 2013;20:599–604.
5. Jauch EC, Saver JL, Adams HP Jr, Bruno A, Connors JJ, Demaerschalk BM, et al. On behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44:870–947.
6. Molina CA, Alexandrov AV, Demchuk AM, Saqqur M, Uchino K, Alvarez-Sabín J. improving the predictive accuracy of recanalization on stroke outcome in patients treated with tissue plasminogen activator. Stroke. 2004;35:151–6.
7. Goyal M, Almekhlafi M, Dippel DW, Campbell BC, Muir K, Demchuk AM, et al. Rapid alteplase administration improves functional outcomes in patients with stroke due to large vessel occlusions. Stroke. 2019;50:645.
8. Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 2014;384:1929–35.
9. Cappellari M, Turcato G, Forlivesi S, Bagante F, Cervellin G, Lippi G, et al. The START nomogram for individualized prediction of the probability of unfavorable outcome after intravenous thrombolysis for stroke. Int J Stroke. 2018;13:700–6.
10. Ploneda Perilla AS, Schneck MJ. Unanswered questions in thrombolytic therapy for acute ischemic stroke. Neurol Clin. 2013;31:677–704.
11. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, et al. On behalf of the American Heart Association Stroke Council: Guidelines for the Early Management of Patients with Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2019;50:e344–418.
12. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24:35–41.
13. Parker S, Ali Y. Changing contraindications for t-PA in acute stroke: review of 20 years since NINDS. Curr Cardiol Rep. 2015;17:81.
14. Muchada M, Rubiera M, Rodriguez-Luna D, Pagola J, Flores A, Kallas J, Sanjuan E, et al. Baseline National Institutes of Health Stroke Scale-Adjusted Time Window for intravenous tissue-type plasminogen activator in acute ischemic stroke. Stroke. 2014;45:1059–63.
15. Van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, Van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke. 1988;19:604–7.
16. Fiorelli M, Bastianello S, von Kummer R, Del Zoppo GJ, Larrue V, Lesaffre E, et al. Hemorrhagic transformation within 36 hours of a cerebral infarct: relationships with early clinical deterioration and 3-month outcome in the European Cooperative Acute Stroke Study I (ECASS I) cohort. Stroke. 1999;30:2280–4.
17. Derex L, Nighoghossian N. Intracerebral haemorrhage after thrombolysis for acute ischemic stroke: an update. J Neurol Neurosurg Psychiatry. 2008;79:1093–9.
18. Wardlaw JM, Murray V, Berge E, Del Zoppo GJ. Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev. 2014;2014: CD000213.
19. Abdel-Monem EF, Afifi FM, Essmat A. Predictors of functional outcome after treatment of acute ischemic stroke. S Can Uni Med J. 2020;23:176–81.
20. Mehrpour M, Shojae SF, Sohrabi A. factors predicting the outcome of intravenous thrombolysis in stroke patients before rtPA administration. Caspian J Intern Med. 2019;10:424–30.
21. Sun F, Liu H, Fu HX, Li CB, Geng XJ, Zhang XX, et al. Predictive factors of hemorrhage after thrombolysis in patients with acute ischemic stroke. Front Neurol. 2020;11: 551157.
22. Elsayed MA, Salah H, Sabbah A, Hatem G, Moawad MK. Early functional outcome after IV rTPA administration in Egyptian acute ischemic stroke patients. Egypt J Neurol Psych Neurosurg. 2019;55:64.
23. Mohamed WS, Abdel Ghaffar AS, Abdel Gawad AE, Agban EL. Short-term outcome in ischemic stroke patients after thrombolytic therapy. Egypt J Neurol Psych, Neurosurg. 2021;57:1.
24. Su Y, Chen X, Ye X, Sun H, Wu F, Dong Q, et al. The value of ADAMTS13 in predicting clinical outcomes in patients with acute ischemic stroke receiving thrombolysis. Front Neurol. 2020;31(11):799. https://doi.org/10.3389/fneur.2020.00799
25. Suengtaworn A, Saposnik G, Hurst CP, Poungvarin N, Nilanont Y. Accuracy of clinical risk scores in predicting post-rtPA, intracerebral hemorrhage in a Thai Cohort. J Med Assoc Thai. 2019;102:1–7.
26. Saposnik G, Gladstone D, Raptis R, Zhou L, Hart RG. Atrial fibrillation in ischemic stroke predicting response to thrombolysis and clinical outcomes. Stroke. 2013;44:99–104.
27. Zhang Y, Cai H, Shu H, He R, Huang X, Song X. Efficacy, influencing factors, and safety of alteplase intravenous thrombolysis in patients with acute ischemic stroke combined with atrial fibrillation. J Chemest 2022; 9909703.
28. Yunzhen Hu, Ji C. Efficacy and safety of thrombolysis for acute ischemic stroke with atrial fibrillation: a meta-analysis. BMC Neurol. 2021;21:66.
29. Kimura K, Iguchi Y, Shibazaki K, Iwanaga T, Yamashita S, Aoki J. IV t-PA therapy in acute stroke patients with atrial fibrillation. J Neurol Sci. 2009;276:6–8.
30. Vemmos KN, Tsivgoulis G, Spengos K, Zakopoulos N, Synetos A, Manios E, et al. U-shaped relationship between mortality and admission blood pressure in patients with acute stroke. J Intern Med. 2004;255:257–65.
31. Okumura K, Ohya Y, Maehara A, Wakugami K, Iseki K, Takishita S. Effects of blood pressure levels on case fatality after acute stroke. J Hypertens. 2005;23:1217–23.
32. Darger B, Gonzales N, Banuelos RC, Peng H, Radecki RP, Doshi PB. Outcomes of patients requiring blood pressure control before thrombolysis with tPA for acute ischemic stroke. West J Emerg Med. 2015;1002:7.
33. Leonardi-Bee J, Bath PM, Phillips SJ, Sandercock PA, IST Collaborative Group. Blood pressure and clinical outcomes in the international stroke trial. Stroke. 2002;33:1315–20.
34. Bhardwaj A, Sharma G, Raina SK, Sharma A, Angra M. Advanced age and higher National Institutes of Health Stroke Scale Score as predictors of poor outcome in ischemic stroke patients treated with alteplase: a study from a tertiary care centre in rural North-west India. J Neurosci Rural Pract. 2017;8:236–40.
35. Novak V, Hu K, Desrochers L, Novak P, Caplan L, Lipsitz L, et al. Cerebral flow velocities during daily activities depend on blood pressure in patients with chronic ischemic infarctions. Stroke. 2010;41:61–6.
36. Gacoń J, Badacz R, Stępień E, Karch I, Enguita FJ, Żmudka K, et al. Diagnostic and prognostic micro-RNAs in ischaemic stroke due to carotid artery stenosis and in acute coronary syndrome: a four-year prospective study. Kardiol Pol. 2018;76:362–9.
37. El-Khawas H, Nasef A, Gaber AD. Admission hyperglycemia in acute ischemic stroke: effects on short term prognosis. Egypt J Neurol Psychiat Neurosurg. 2006;43:603–13.
38. Saposnik G, Guzik AK, Reeves M, Ovbiagele B, Johnston SC. Stroke prognostication using age and NIH stroke scale: span-100. Neurology. 2013;80:21–8.
39. Chiara B, Guillaume C, Gwendoline R, Marie-Helene M, Laurent S. Predictors of clinical outcome after intravenous thrombolysis in ischemic stroke without large vessel occlusion: the role of admission glycemia. M J E-Med. 2018;3:030.
40. Ali SF, Siddiqui K, Ay H, Silverman S, Singhal A, Viswanathan A, et al. Baseline predictors of poor outcome in patients too good to treat with intravenous. Thrombolysis Stroke. 2016;47:2986–92.

41. Matsuo R, Ago T, Kiyuna F, Sato N, Nakamura K, Kuroda J, et al. Smoking status and functional outcomes after acute ischemic stroke. Stroke. 2020. https://doi.org/10.1161/STROKEAHA.119.027230.
42. König IR, Ziegler A, Bluhmki E, Hacke W, Bath PM, Sacco RL, et al. Predicting long-term outcome after acute ischemic stroke: a simple index works in patients from controlled clinical trials. Stroke. 2008;39:1821–6.
43. Heuschmann PU, Kolominsky-Rabas PL, Roether J, Misselwitz B, Lowitzsch K, Heidrich J, et al. Predictors of in-hospital mortality in patients with acute ischemic stroke treated with thrombolytic therapy. JAMA. 2004;292:1831–8.
44. Sylaja PN, Cote R, Buchan AM, Hill MD, Canadian Alteplase for Stroke Effectiveness Study Investigators. Thrombolysis in patients older than 80 years with acute ischaemic stroke: Canadian alteplase for stroke effectiveness study. J Neurol Neurosurg Psychiatry. 2006;77:826–9.
45. Roquer J, Rodriguez-Campello A, Cuadrado-Godia E, Giralt-Steinhauer E, Jiménez-Conde J, Dégano IR, et al. Ischemic stroke in prediabetic patients. J Neurol. 2014;261:1866–70.

Publisher's Note